

REMARKS

The undersigned, on behalf of the Applicants, would like to thank Examiner Hui for the telephonic interview granted on March 23, 2005. It was agreed that all claims except 22 and 23 would be canceled. Claims 22 and 23 have been allowed.

Amend page 6 of the specification as shown.

Cancel Claims 1-21 and 24-26 without prejudice.

Amend Claims 22 and 23 as shown on the list of Claims in this response.

The specification has been amended on page 6 by replacing the paragraph encompassed by lines 15-24. The purpose of this amendment is to correct the formula of lecithin set forth on line 16 of the original paragraph. The formula of lecithin in the original paragraph is an original error as is shown by the correct formula which is given in The Merck Index, Tenth Edition, Paragraphs 5271-72, 1983 (copy attached).

Claim 22 has been amended by correcting the amount of glycerine recited for the composition of Example 1 from 24mg to 2.4mg.

Claim 23 has been amended by correcting the amount of glycerine recited for the composition of Example 3 from 24mg to 2.4mg.

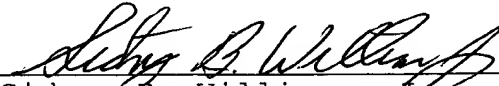
The purpose of the amendments to claims 22 and 23 is to correct an obvious typographical error. These amendments do not constitute new matter because one skilled in the art would readily recognize that the amount of glycerine described in Examples 1 and 3 are out of line with the amounts of glycerine described in Examples 2, 4 and 5. This would be obvious to one skilled in the art because the amounts of other components of Examples of 2, 4 and 5 are identical to the other components of Examples 1 and 3. *In re Oda et al*, 170 USPQ 268 (CCPA-1971).

Entry of the amendment is respectfully requested because it (1) reduces the number of issues, (2) reduces the number claims, (3) does not introduce new matter into the case and

(4) puts the case in better condition for consideration on appeal.

In view of the cancellation of Claims 1-21 and 24-26 and the amendments of Claims 22 and 23, withdrawal of the rejection and expeditious passage of this case to issue is respectfully solicited.

Respectfully submitted,


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Reg. No. 43 977
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Encl: The Merck Index, Tenth Edition, Paragraphs 5271-72, 1983
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np reverts to PbO. d 9.53. mp 110°. Sol in acetic acid, dil HNO₃, i hydroxides. LD₅₀ i.p. in rats, k. Ind. Med. 107 Ind. Hyg. 107. **TRADE MARK**

g dust. Wear dust mask ap. Mines for this purpose. Wash smoking. Keep away from food.

s; preparing soln of lead subacetate; flux for painting on porcelain dishes; with glycerol as metal colors on brass and bronze; color-stances, e.g., hair, nails, wool, use shell and horn; pigment for oil; in assay of gold and silver

Pb_2O_3 ; mol wt 331.23. N 8.46%, NO_2 . cent-crystals. d 4.53. **Poisonous!** LD₅₀ i.p. in guinea pigs: 0.75 ml boiling water, in 2500 methanol; insol in concd HNO₃. pH of 20% aq soln at 25° =

special explosives; as mordant in dyes; mordant for staining horn, dye industry; sensitizer in photo. been used as a caustic in equine

ic acid lead salt. Approx $\text{Pb}(\text{C}_2\text{H}_3\text{O}_2)_2$

Insol in water; sol, when fresh, urpentine. LD orally in guinea of *Toxicology* vol. 1, W. S. Spector, Ed. (Academic Press, 1956) pp 176-177. eme pressure lubricants.

O_2Pb ; mol wt 295.23. C 8.14%, O_2 . dec at 300°. d 5.28. **Poisonous!** HNO₃, fixed alkali hydroxides;

O_2Pb_2 ; mol wt 811.54. O 10.14%, $\text{Pb}_2(\text{PO}_3)_2$. mp 1014°. **Poisonous!** Insol in fixed alkali hydroxides. been listed as a carcinogen in the *Carcinogens* (NTP 81-43, Dec. 1971).

PbSe ; mol wt 350.17. O 18.28%, SeO_4 . Prepd by adding a soln of selenic acid to a soln of lead acetate. Lenher, Kao, *J. Am. Chem. Soc.* 53, 1511 (1931).

d₂₀ 6.37. Dec by heat. Sol in

PbSe ; mol wt 334.17. O 14.36%, SeO_3 . Prepd by adding selenious acid to a soln of lead chloride or nitrate. vol. X, 833 (1930). at 500° forming a yellow liquid, giving off selenium oxide. Very sublimely dec by boiling sulfuric acid.

Lead trioxide; plumbous plumbite. O 10.38%, Pb 89.62%. Pb_2O_3 converted at 370° in air to Pb_3O_4 . Insol in water; dec by concd HCl on of Cl or oxygen, respectively.

iosulfate. Lead sodium hyposulfite. Na 14.47%, O 22.66%, $\text{Pb}(\text{S}_2\text{O}_3)_2$. **Poisonous!** Sparingly sol in solns.

5260. Lead Stearate. Stearic acid lead salt. Approx $\text{Pb}(\text{C}_{17}\text{H}_{33}\text{O}_2)_2$. (White powder, mp about 125°. **Poisonous!** Insol in water; sol in hot alcohol.

USE: In extreme pressure lubricants; as drier in varnishes.

5261. Lead Subacetate. Lead monosubacetate; monobasic lead acetate. $\text{C}_4\text{H}_7\text{O}_5\text{Pb}$; mol wt 807.75. C 5.95%, H 1.25%, O 15.85%, Pb 76.96%. $\text{Pb}(\text{C}_2\text{H}_3\text{O}_2)_2 \cdot 2\text{Pb}(\text{OH})_2$.

White, heavy powder. **Poisonous!** Sol in 16 parts cold, 4 parts boiling water with alkaline reaction. On exposure to air absorbs CO₂ and becomes incompletely sol. **Keep well closed.**

USE: In sugar analysis to remove coloring matters, etc., from solns before polarizing; for clarifying and decolorizing other solns of organic substances.

5262. Lead Sulfate. O_2PbS ; mol wt 303.28. O 21.10%, Pb 68.32%, S 10.57%. PbSO_4 . Occurs as the minerals: *anglesite*, *lanarkite*.

White, heavy, cryst powder. **Poisonous!** d 6.2. mp 1170°. Sol in about 2225 parts water; more soluble in dil HCl or HNO₃, less in dil H₂SO₄; sol in NaOH, ammonium acetate or tartarate soln; sol in concd hydrochloric acid; insol in alcohol. LD₅₀ i.p. in guinea pigs: 290 mg/kg. *Handbook of Toxicology* vol. 1, W. S. Spector, Ed. (Saunders, Philadelphia, 1956) pp 178-179.

USE: Instead of white lead as pigment; with zinc in galvanic batteries; manuf minium, in lithography; preparing rapidly drying oil varnishes; weighting fabrics.

5263. Lead Sulfide. PbS ; mol wt 239.28. Pb 86.60%, S 13.40%. Occurs as the mineral *galena*.

Black powder. Insol in water; sol in HNO₃, hot, dil HCl. LD₅₀ i.p. in rats: 1.8 g/kg, Bradley, Fredrick, *Ind. Med.* 10, *Ind. Hyg. Sect.* 2, 15 (1941).

USE: Glazing earthenware.

5264. Lead Telluride. PbTe ; mol wt 334.82. Pb 61.89%, Te 38.11%. Found in nature as the mineral *altaite*. Prepd from lead nitrate, sodium carbonate and powdered tellurium. Montignie, *Bull. Soc. Chim. France* 1947, 750. Prepn of single crystals by heating stoichiometric quantities of the elements in a graphite cup or fused quartz tube: Brady, *J. Electrochem. Soc.* 101, 466 (1954).

Silver-gray cubic crystals. d₂₀ 8.16. mp 905°. Most of the crystal is p-type, the n-type material being present in the surface layer. Energy gap 0.27 eV. Electron mobility 2240 cm²/volt-sec. Hole mobility 860 cm²/volt-sec. Resistivity 0.005 ohm-cm (p-type), 0.00090 ohm-cm (n-type). Not attacked by hydrochloric, hydrofluoric, perchloric and acetic acids or their mixtures; not attacked by solns of 30% potassium hydroxide or of alkali metal sulfides. Dil nitric acid turns the surface black, while concd nitric acid produces lighter gray surface and turns the black surface to gray. Hot concd sulfuric acid produces a reddish-violet surface.

USE: In photoconductor cells; in semiconductor research.

5265. Lead Tetraacetate. $\text{C}_8\text{H}_{12}\text{O}_8\text{Pb}$; mol wt 443.39. C 21.67%, H 2.73%, O 28.87%, Pb 46.73%. $\text{Pb}(\text{CH}_3\text{COO})_4$. Prepd from Pb_3O_4 and glacial acetic acid preferably in the presence of some acetic anhydride: Dimroth, Schweizer, *Ber.* 56, 1375 (1923); Bailar, *Inorg. Syn.* 1, 47 (1939); Baudler in *Handbook of Preparative Inorganic Chemistry* vol. 1, G. Brauer, Ed. (Academic Press, New York, 2nd ed., 1963) p 767. Prepn by electrolysis: Fioshion, Gus'kov, *Dokl. Akad. Nauk SSSR* 112, 303 (1957). C.A. 51, 16146 (1957); Sataev et al., *Khim. Prom. (Moscow)* 46, 892 (1970). C.A. 74, 49005x (1971). Reviews of prepn and use as oxidizing agent: Criegee, "Oxidations with Lead Tetraacetate" in *Oxidation in Organic Chemistry*, Part A, K. B. Wiberg, Ed. (Academic Press, New York, 1965) pp 277-366; Zyka, *Pure Appl. Chem.* 13, 569-581 (1966).

Colorless monoclinic prisms from glacial acetic acid. Turns pink easily. Unstable in air. Hydrolyzed by water with the formation of brown lead dioxide and acetic acid. Avoid contact with skin. d₄ 2.228. mp 175-180°. Sol in hot glacial acetic acid, benzene, chloroform, tetrachloroethane, nitrobenzene. Dissolves in concd halogen acids with the formation of haloplumbic acids, H_2PbX_6 . The dry material can be stored in sealed, evacuated ampuls.

USE: Selective oxidizing agent in organic syntheses: Criegee, *Angew. Chem.* 53, 321 (1940); *Newer Methods of Preparative Organic Chemistry* (Interscience, N. Y., 1948) pp 1-17.

5266. Lead Tetrafluoride. Plumbic fluoride. F_4Pb ; mol wt 283.21. F 26.84%, Pb 73.16%. PbF_4 . Prepd by passing fluorine diluted with CO₂ or N₂ over PbF_2 at 300°. v. Wartenberg, *Z. Anorg. Allgem. Chem.* 244, 339 (1940). Review: Kemmitt, Sharp, *Advan. Fluorine Chem.* 4, 187 (1965).

White, tetragonal crystals, d 6.7. mp about 600°. Readily hydrolyzes and turns brown (forms PbO_2) in the presence of moisture.

USE: Has been proposed as a fluorinating agent for hydrocarbons.

5267. Lead Tetroxide. Lead oxide red; red lead; minium; lead orthoplumbate; mineral orange; mineral red; Paris red; Saturn red; C.I. Pigment Red 105; C.I. 77578. O_4Pb_3 ; mol wt 685.63. O 9.33%, Pb 90.67%. Pb_3O_4 . The article of commerce contains about 90% Pb_3O_4 , the remainder being chiefly lead monoxide. Prepn: M. Baudler in *Handbook of Preparative Inorganic Chemistry* vol. 1, G. Brauer, Ed. (Academic Press, New York, 1963) pp 755-757. Structure: S. T. Gross, *J. Am. Chem. Soc.* 65, 1107 (1943). Review: Mellor's vol. 7 (1930) pp 672-680.

Bright-red, heavy powder. **Poisonous!** Dec at about 500° with evolution of oxygen. d 9.1. Insol in water or alcohol; sol in excess glacial acetic acid, in hot HCl with evolution of Cl₂ in dil HNO₃ in presence of H₂O₂. LD₅₀ i.p. in guinea pigs: 220 mg/kg. *Handbook of Toxicology* vol. 1, W. S. Spector, Ed. (Saunders, Philadelphia, 1956) pp 176-177.

USE: Plasters and ointments; manuf colorless glass; glaze for faience; flux for porcelain painting, protective paint for iron and steel; oil-color for ship paints, varnishes; coloring rubber; cement for glass, gas and steam pipes; storage batteries; pencils for writing on glass; manuf lead peroxide, matches.

5268. Lead Thiocyanate. Lead sulfocyanate. $\text{C}_2\text{N}_2\text{PbS}_2$; mol wt 323.38. C 7.43%, N 8.66%, Pb 64.08%, S 19.83%. $\text{Pb}(\text{SCN})_2$. Prepn: Gardner, Weinberger, *Inorg. Syn.* 1, 85 (1939).

White, odorless powder. d 3.82. **Poisonous!** Sol in about 200 parts cold, 50 parts boiling water; also sol in alkali hydroxide and thiocyanate solns.

USE: Reverse dyeing with aniline black; manufacture of safety matches and cartridges.

5269. Lead Tungstate(VI). O_4PbW ; mol wt 455.07. O 14.06%, Pb 45.53%, W 40.41%. PbWO_4 . Occurs as the minerals *raspite*, *scheelite*, *stolzite*.

White powder. Insol in water or cold HNO₃; sol in fixed alkali hydroxide solns.

5270. Lead Vanadate(V). Lead metavanadate. O_3PbV_2 ; mol wt 405.11. O 23.70%, Pb 51.15%, V 25.15%. $\text{Pb}(\text{VO}_3)_2$. Yellow powder, insol in water; dec by HNO₃.

USE: Manuf other vanadium compds; as pigment.

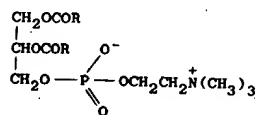
5271. Lecithin. Phosphatidylcholine; Lecithol; Vitellin; Kelecine; Granulestin. Phosphatide found in all living organisms (plants and animals). Significant constituent of nervous tissue and brain substance. A mixture of the diglycerides of stearic, palmitic, and oleic acids, linked to the choline ester of phosphoric acid. Commercial grades contain 2.2% P. Isolated from eggs: Sinclair, *Can. J. Res.* 26B, 777 (1948). Product of commerce is predominantly soybean lecithin obtained as a by-product in the manuf of soybean oil: Stanley in K. S. Markley, *Soybeans* vol. II (Interscience, New York, 1951) pp 593-647. Soybean lecithin contains palmitic acid 11.7%, stearic 4.0%, palmitoleic 8.6%, oleic 9.8%, linoleic 55.0%, linolenic 4.0%, C₂₀ to C₂₂ acids (includes arachidonic) 5.5%. Synthesis of a mixed acid α -lecithin: de Haas, van Deenen, *Tetrahedron Letters* 1960 (no. 9), 1. Synthetic L- α -(distearoyl)lecithin is identical with hydrogenated egg yolk lecithin and L- α -(dipalmitoyl)lecithin is identical with a natural phosphatide of brain, lung, and spleen. (See also Phosphatidic Acid.) Commercial grades of natural lecithin are reported to contain a potent vasodepressor substance: McQuarrie, Andersen, U.S. pat. 2,931,818 (1960 to Cutter Labs.). Comprehensive monograph: G. B. Ansell, J. N. Hawthorne, *Phospholipids* (Elsevier, New York, 1964) 439

Consult the cross index before using this section.

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pp; J. Eichberg, "Lecithin" in Kirk-Othmer *Encyclopedia of Chemical Technology* vol. 14 (Wiley-Interscience, New York, 3rd ed., 1981) pp 250-269.



Waxy mass when the acid value is about 20. Pourable, thick fluid when the acid value is around 30. Color is nearly white when freshly made, but rapidly becomes yellow to brown in air. d_4^{25} 1.0305. Iodine value 95; saponification value 196. Insoluble but swells up in water and in NaCl soln forming a colloidal suspension. Soluble in about 12 parts cold, abs alcohol; sol in chloroform, ether, petr ether, in mineral oils and fatty acids; sparingly sol in benzene. Insol in acetone; practically insol in cold vegetable and animal oils.

USE: Edible and digestible surfactant and emulsifier of natural origin. Used in margarine, chocolate and in the food industry in general. In pharmaceuticals and cosmetics. Many other industrial uses, e.g. treating leather and textiles.

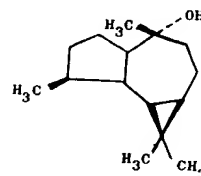
THERAP CAT: Lipotropic.

5272. Lectins. Agglutinins; affinities; phytoagglutinins; phasins; protectins. A group of proteins, widely distributed in nature, that have the ability to agglutinate erythrocytes and many other types of cells. Although their existence has been known since 1899, when Stillmark isolated a hemagglutinin from castor beans, the term "lectin" (from the Latin *legere*, to choose) was first introduced by W. C. Boyd and E. Slaplegh in *Science* 119, 419 (1954). It is now used to designate "a sugar-binding protein or glycoprotein of non-immune origin which agglutinates cells and/or precipitates glycoconjugates", I. J. Goldstein *et al.*, *Nature* 285, 66 (1980). Lectins are found primarily in seeds of plants, but also occur in roots, leaves and bark. In addition, they are present in invertebrates such as clams, snails, and horseshoe crabs, and in several vertebrate species. The term *phytohemagglutinin* is used to refer to plant lectins. Important members of the lectin family include concanavalin A, abrin, ricin, *q.q.v.*, as well as *soybean agglutinin* or *SBA* and *wheat germ agglutinin* or *WGA*. Lectins vary considerably in chemical and physical properties; only a limited number have been purified. Mol wts of 17,000 to 400,000 have been reported and most lectins have been found to contain Mn^{2+} and Ca^{2+} . Nearly all lectins can be inhibited by free oligo- or monosaccharides of appropriate specificity. Although their physiological functions in plants or in other organisms are unknown, lectins exhibit a variety of unusual biological properties. Some are specific in their reactions with human blood groups; some induce mitosis in lymphocytes. WGA from wheat germ lipase has been shown to agglutinate mouse tumor cells more readily than cells from normal tissue: J. C. Aub *et al.*, *Proc. Nat. Acad. Sci. USA* 50, 613 (1963); M. M. Burger, A. R. Goldberg, *ibid.* 57, 359 (1967). Soybean agglutinin and concanavalin A have been shown to agglutinate cell lines transformed by viral or chemical carcinogens: M. Inbar, L. Sachs, *Nature* 223, 710 (1969); *idem*, *Proc. Nat. Acad. Sci. USA* 63, 1418 (1969); B. A. Sela *et al.*, *J. Membrane Biol.* 3, 267 (1970). Soybean agglutinin has also been used in bone marrow transplants in patients with severe combined immunodeficiency: Y. Reisner *et al.*, *Blood* 61, 341 (1983). Reviews: N. Sharon, H. Lis, *Science* 177, 949-955 (1972); *idem*, *Ann. Rev. Biochem.* 42, 541-574 (1973); L. Sequeira, *Ann. Rev. Phytopathol.* 16, 453-481 (1978). Book: *Lectins: Biology, Biochemistry, Clinical Biochemistry* vol. 1, T. C. Bog-Hansen, Ed. (de Gruyter, New York, 1981) 414 pp.

USE: As tools for studying cell surface properties; in cancer research.

5273. Ledol. Decahydro-1,1,4,7-tetramethyl-1H-cyclopropylazulen-4-ol; "Ledum camphor". $\text{C}_{15}\text{H}_{26}\text{O}$; mol wt 222.36. C 81.02%, H 11.79%, O 7.20%. Occurs in the essential oil from leaves of *Ledum palustre* L.: Grassmann, *Repert. Pharm.* 38, 53 (1931); Hjelt, *Ber.* 28, 3087 (1895); from

L. groenlandicum Veder; *L. columbianum* Piper, *Ericaceae*: Cain, Lynn, *J. Am. Pharm. Assoc.* 23, 666 (1934); Penfold, *J. Proc. Roy. Soc. N.S. Wales* 59, 206 (1925). Structure: Büchi *et al.*, *Tetrahedron Letters* 1959 (no. 6), 14; Graham *et al.*, *Aust. J. Chem.* 13, 372 (1960). Stereochemistry: Dolejs, Sorm, *Tetrahedron Letters* 1959 (no. 17), 1.

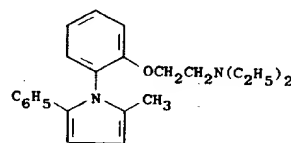


Needles from alc, mp 104-105°. Sublimes easily, even below the mp. $b.p_{760}$ 292°. n_D^{20} 1.4667. $[\alpha]_D^{20} +28^\circ$ ($c = 10$ in chloroform). Practically insol in water. Sol in alc (about 10% w/v). Soluble in other organic solvents.

Chromate, $\text{C}_{30}\text{H}_{50}\text{O}_4\text{Cr}$, ruby-red prisms, mp 92°. $[\alpha]_D^{20} +30^\circ$ ($c = 2$ in chloroform).

5274. Leghemoglobin. *Legoglobin*. Hemoglobin-like red pigment present in the root nodules of leguminous plants. Isolation from soya beans: Keilin, Wang, *Nature* 155, 227 (1945); Appleby, *Biochim. Biophys. Acta* 60, 226 (1962). Mol wt is approx one-fourth that of hemoglobin: Ehrenberg, Ellfolk, *Acta Chem. Scand.* 17, S343 (1963). Resolved into four components on DEAE-cellulose column: Ellfolk, *ibid.* 14, 609 (1960). Suggested to act as an oxido-reduction catalyst in the symbiotic nitrogen fixation: *idem*, *ibid.* 15, 975 (1961). Primary structure of soybean leghemoglobin: Ellfolk, Sievers, *ibid.* 25, 3532 (1971).

5275. Leiopyrrole. *N,N*-Diethyl-2-[2-(2-methyl-5-phenyl-1H-pyrrol-1-yl)phenoxy]ethanamine; 1-[o-(2-diethylaminoethoxy)phenyl]-2-methyl-5-phenylpyrrole; 2-methyl-1-(2-β-diethylaminoethoxyphenyl)-5-phenylpyrrole; DV 714. $\text{C}_{23}\text{H}_{29}\text{N}_2\text{O}$; mol wt 348.47. C 79.27%, H 8.10%, N 8.04%, O 4.59%. Preparation: Buu-Hoi *et al.*, *J. Med. Pharm. Chem.* 1, 23 (1959).



Hydrochloride, $\text{C}_{23}\text{H}_{29}\text{ClN}_2\text{O}$, *Leioplegil*. Needles from carbon tetrachloride, mp 138°. (Base, $b.p_{13}$ 232°; n_D^{20} 1.6025.) Readily sol in water; aq soln turns yellow on exposure to air or light.

THERAP CAT: Antispasmodic.

5276. Lemon Peel. Outer rind of fresh ripe fruit of *Citrus limon* (L.) Risso (*C. medica* var. *limon* L.), *Rutaceae*. *Habit.* Northern India; cultivated in California, West Indies, Italy, Spain. *Constit.* Volatile oil, hesperidin, bitter extractive.

USE: As a flavor in medicines; also in beverages, confectionery, and cooking.

5277. Lenacil. 3-Cyclohexyl-6,7-dihydro-1H-cyclopentapyrimidine-2,4-(3H,5H)-dione; 3-cyclohexyl-5,6-trimethylencuracil; 3-cyclohexyl-1,5,6,7-tetrahydro-2H-cyclopentapyrimidine-2,4(3H)-dione; du Pont 634; Venzar. $\text{C}_{13}\text{H}_{18}\text{N}_2\text{O}_2$; mol wt 234.29. C 66.64%, H 7.74%, N 11.96%, O 13.66%. Prepn: Senda, Fujimura, Japan. pat. 4892('62).

